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Editorial comment

Cancer-pain intractable to high-doses systemic opioids can be relieved by intraspinal local anaesthetic plus an opioid and an alfa$_2$-adrenoceptor agonist

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In this issue of the *Scandinavian Journal of Pain* we publish a second highly important article this year (2017) on the high efficacy and safety of intrathecal analgesia by the three experienced pain clinicians Lauri Kiehelä, Katri Hamunen, and Tarja Heiskanen at the Division of Pain Medicine at the Department of Anaesthesiology, Intensive Care and Pain Medicine in Helsinki [1]. They report their successful results managing with spinal multimodal analgesia 60 patients with terminal cancer pain intractable with systemic opioids and co-medications [1]. Mastenbroek and co-workers published a similar report on terminal cancer-patients with otherwise intractable pain who received successful intrathecal analgesia [2]. These reports are observational studies in an area of pain and palliative medicine that cannot be studied with RCTs, i.e. traditional randomized and controlled studies, double blinded, with placebo or other active therapy [3].

1. Terminal cancer-patients suffering from pain that is intractable with high dose systemic opioids do better with intrathecal multimodal analgesia

These two reports are extremely important because authoritative palliative care authors in 2015, finding no "evidence" from low quality RCTs, concluded that intraspinal analgesia with opioids should not be used for cancer-pain [4]. This has resulted in therapeutic nihilism among some palliative care teams without a qualified anaesthesiologist pain clinician, reducing referrals for intraspinal analgesia from palliative units to pain-sections and departments of pain management [3].

It should be noted that 16 of the 60 patients in the Helsinki study had epidural analgesia, and only 8 (50%) had satisfactory relief of their pain, whereas 70% of the 44 who received intrathecal analgesia had satisfactory pain relief [1]. This confirms other reports that intrathecal administration of a local anaesthetic drug, an opioid, and an alfa$_2$-adrenoceptor-agonist will relieve even the most opioid-intractable cancer pain conditions [2,3]. Whereas clonidine is a more potent and more specific alfa$_2$ agonist, it does cause hypotension and sedation. This can be avoided by using adrenaline (epinephrine) instead of clonidine [4,5].

An important observation by Kiehelä and co-workers is that it is important to place epidural or intrathecal catheters at thoracic or high lumbar spinal levels in order to avoid leg weakness and paralysis from the local anaesthetic component [1,5]. A lower lumbar insertion will cause motor-block of all cauda equine nerve-roots, resulting in leg paralysis, and urinary, and sometimes even rectal incontinence.

The starting dose they estimated by using a systemic morphine to intrathecal equivalent-analgesic ratio of 100 to 1 and adding 30 mg of clonidine and 7.5 mg of bupivacaine [1]. When pain relief was not satisfactory, catheter dislocation was the most common reason.

Another important confirmatory observation by the Helsinki-pain clinicians is that when patients have been receiving intravenously high doses of opioids, with a median of almost 900 mg oral morphine equivalents in their study, when pain is relieved with intrathecal or epidural multimodal analgesia, it is imperative that the patients continue with a tapering dose opioids systemically. Otherwise, very unpleasant withdrawal symptoms will make the patients extremely miserable [1].

For the patients in whom systemic opioids were discontinued after IT catheter placement and titration ($n = 18$), the conversion ratio from systemic to IT opioid ranged from 18:1 to 400:1, being on average 152:1. This finding demonstrates that careful individual titration is necessary. For the initial intrathecal infusions, the authors suggest the morphine dose calculated using an oral to intrathecal ratio of 100:1 in most patients.

IT catheters were placed on average 98 days before death, the average duration of IT treatment was 58 days, and dislocation was a frequent cause of discontinuation. We agree with the authors that this calls for technical improvements. The solution could be use of implantable subcutaneous ports or pumps. That would most

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probably reduce dislocation, make treatment for a longer period possible and also allow for IT breaks in patients with fluctuation symptoms.

2. Intra-thecal analgesia or terminal palliative sedation?

The only remaining alternative when systemic multimodal analgesia fails and intraspinal analgesia is not available, is palliative sedation, i.e. giving the patient deep enough intravenous sedation so that the patient remains unconscious and unaware of the pain-condition caused by an invasive and metastasizing malignant tumour. This is synonymous with prolonged intravenous general anaesthesia with all the ethical and practical issues involved.

3. Availability of spinal analgesia for advanced cancer and difficult to relieve pain

The Helsinki pain clinicians estimated that only 0.5% of patients with advanced cancer-pain received effective intraspinal analgesia in Helsinki, and they believe this is partly due to the unfamiliarity of spinal analgesia among health care providers as an advanced method of treatment for cancer pain, and the perceived limited availability of the method.

The percentage of cancer patients where systemic multimodal analgesia fail, ranges from 1% to 20% [1,6,7].

Conflict of interest

None declared.

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